Growth Control and Disease Mechanisms in Computational Embryogeny

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ABSTRACT

This paper presents novel approach to applying growth control and diseases mechanisms in computational embryogeny. Our method, which mimics fundamental processes from biology, enables individuals to reach maturity in a controlled process through a stochastic environment. Three different mechanisms were implemented; disease mechanisms, gene suppression, and thermodynamic balancing. This approach was integrated as part of a structural evolutionary model. The model evolved continuum 3-D structures which support an external load. By using these mechanisms we were able to evolve individuals that reached a fixed size limit through the growth process. The growth process was an integral part of the complete development process. The size of the individuals was determined purely by the evolutionary process where different individuals matured to different sizes. Individuals which evolved with these characteristics have been found to be very robust for supporting a wide range of external loads.

Keywords

Genetic Algorithm, Indirect Encoding, Stresses, Finite Element, Artificial Cell

1. INTRODUCTION

Natural evolution has produced systems of fantastic complexity, robustness and adaptability. Recent research has shown that it is the combination of both evolution and development processes that have produced these remarkable results [3, 8]. Evolution does not act directly on the configurations of adult phenotypes, rather it successively alters and revises the *rules* that guide the growth of a zygote into an embryo and its further development into an adult. In nature, *rules* are encoded in the patterns of amino acids in genes, which regulate the production of protiens, and hence the growth and development of the organism. *Embryogeny* is the process of growth by which a genotype develops into a phenotype, and is central to the emerging understanding of the relationship between evolution and development.[1] DNA contains a set of instructions for the development process while the environment provides inputs that regulate the instructions [10]. Natural evolutionary processes refine the sets of rules, in the form of genes, which result in adult forms. Natural selection acts upon the phenotypes, thus rewarding sets of rules that produce fit individuals. The *indirect* character of the encoding of genetic information in natu-

[1]It should be noted that the correct term is *embryogeny*, which refers to the process, rather than the oft-misused term *embryology*, which refers to the science of studying embryos. [2]

ral systems and the inter-relationship between the evolution of rules and the growth and development of adult forms, have been responsible for the diversity, complexity, modularity, robustness, and adaptability in the natural world [11, 4]. One of the major challenges in computational embryogeny is the controlled growth of an individual during the development process. Most computational embryogeny uses the notion of cell division operations in different ways. This may lead to a scenario where cells constantly divide unless some upper limit has been predefined. In this case the developmental stage is artificially stopped. In this paper we will present a novel approach which mimics the fundamental processes in nature and helps an organism to reach a limited size even in a high volatility environment. It has been observed that phenotypes in nature tend to grow rapidly during early stages of development and grow at a slowly decaying rate as they reach maturity [6]. This kind of behavior is common to all plants and organisms. The immune system has a major contribution to controlling the development process in organisms [1]. One of the mechanism it uses is gene suppression. Under some conditions one gene may turn off other genes. For example tumor suppression genes turn off other genes that produce tumor cells [9]. The immune system is also responsible for attacking different kinds of diseases. Diseases are defined as an abnormal condition within an organism. Our model mimics both mechanisms. We have included "veto" genes which may suppress the activity of other genes. These genes provide the evolutionary algorithm an ability to evolve control systems which may limit the size of the phenotype. The concept of diseases has also been modeled. In a similar way to biology we have defined abnormality scenarios as diseases. If the immune system fails to repair these abnormal scenarios, the phenotype is eliminate from the population. The size of an organism is also limited by thermodynamic constraints. Following the first law of thermodynamics, there is a balance between the energy generated by an organism to maintain an existing body mass and the energy required to create a new body mass. This fundamental law may introduce a crude upper bound to the size of the phenotype. Using this notation in our model, we were able to create very weak upper bounds on the sizes of our individuals. These bounds do not alter the growth process and, in fact, new mass can still be created at the expense of the existing mass. The paper will start with a short introduction to an artificial model, the definition of genes, morphogenes and the engineering aspects of the model. An explanation of the modeling process of all three mechanism will follow, with some emphasis on how this approach may be used in other computational embryogeny models. The results section will demonstrate the necessity of this approach to produce robust individuals. We claim that there is a correlation between the ability of an individual to developed through control of the process and its performance in the population. In the conclusion we will summarize the reasons we think these mechanisms are crucial in computational embryogeny and how this approach may lead to using computational embryogeny for the synthesis of high performance structures.

2. ARTIFICIAL MODEL

In the work reported here, an artificial embryogeny of structures has been created. The two critical fundamental elements of this work are: the selection of the artificial cell (the basic structural element) comprising each individual; and, the artificial genes (the rules) which are evolved into the genetic information of each individual. The genetic information of an individual is shared by all of its cells. Each individual cell executes its rules until a mature structure is formed. Once maturity is reached, an evaluation scheme determines the fitness (performance) of the structure. Evolutionary operations (selection, crossover, and mutation) alter and refine the genetic information in a population of individuals over multiple generations. The results are structures that meet the desired performance goals.

2.1 Rules

Mimicking nature, the basic structure of a gene is an *if*-conditional *then*-action rule.

2.2 Actions

Mimicking natural embryogeny, every 3-D region can deform according to nine different geometric operations: one for isotropic growth, two for anisotropic growth (B), three for shear (S) and three for rotation [5]. These are illustrated

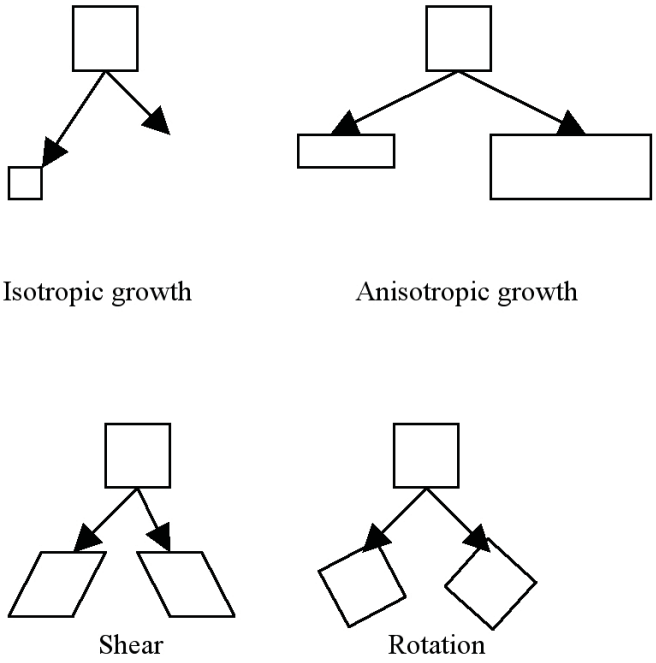


Figure 1: The four basic geometric operations observed in sub-regions of plants.

in Figure 1. In the artificial embryogeny presented here, the geometric operations (excluding the three for rotation) are defined as actions, and as with natural embryogeny, every geometric operation is assigned a unique alphabetic letter.

In addition to the geometric operation actions, cell-type actions are defined, as shown in Table 3. These actions are the three basic operations that occur in the developmental process of every biological structure, including: cell division: cell death and cell differentiation. Cell division splits the cell into two equally sized cells, such that the total volume of the divided cells remains the same as that of the initial single cell. Cell death causes a cell to be removed from the model. Cell differentiation alters the material properties of a cell [7].

2.3 Environment

The environment in which the individuals are grown contains factors which every cell can sense, and which may affect the way genes are expressed. The relationship between the information that cells receive from the environment and the development of the phenotype is not predetermined. Rather, conditionals are available to the evolutionary process that sense the concentration or gradient of each morphogen. In this way, the evolutionary process establishes the relationship between information and growth and development.

In the artificial embryogeny presented here, two kinds of morphogens are present. The first represents a load that is to be supported by the phenotype. The morphogen, representing the load, is produced continuously at the location where the load is to be supported and diffuses through space, impinging on the walls of each cell. The second morphogen represents the surface of the ground, to which cells adhere when they intersect the surface.

As the phenotype is being grown, it is evaluated by means of a finite element analysis to determine the pattern of mechanical stresses and deformations in the phenotype [13]. Every cell is an extended 3-D non-orthogonal finite brick element. Therefore, the structure and the mesh are identical, and are evolved simultaneously during growth and development. The methodology avoids the many complexities related to mesh generation. Since the topology of the phenotype changes during growth and development, the finite element analysis is performed at every time step. Cells also maintain information relating to their size, age, and distance from neighboring cells. Each type of information available to each cell is identified by a lower case alphabetic character, shown in Table 4.

2.4 Genome Structure

The genome contains words which contain genes with their corresponding letters (Tables 4 through 3). Every word starts with the letter "R" which indicates the number of times the particular word will be executed. The letter "Z" indicates the beginning of the word. The genes contain operations, parameters (*e.g., morphogen concentration or gradient*) and coefficients. Similar to transcription factors in nature, coefficients are numbers between zero and one, that scale an effect proportional to the chemical to which they refer.

For instance the word "R1ZC10i" corresponds to: R1 repeat once; Z word boundary indicator; C10i cause the cell to grow isotropically by 10% based on the load morphogen concentration that was measured by that cell.

3. CONTROL MECHANISMS

3.1 Conditionals

The conditional artificial genes are "veto" or "suppression" genes. These genes affect other genes only at the genome level, by turning actions off or on according to whether the conditional test is satisfied or not. Veto genes that switch regulatory mechanisms on or off have been observed in biology [3], for example tumor suppression genes that turn off other genes that produce tumor cells [9].

3.2 Metabolism and Thermodynamics

A thermodynamic energy consideration is present in the model which balances the maintaining of the organism mass with the creation of new mass [12]. The amount of energy E_c that each cell may consume, in a given time step Δt, is proportional to its metabolic rate B_c. Part of this energy is used for maintaining the existing phenotype while the remaining energy may be used for creation of new mass, as shown in Equation 1,

$$E_c = E_0 B_c \Delta t \tag{1}$$

.

The cell's metabolic rate is proportional to the size of the phenotype S and can be determined using Kleinberg's law, given in Equation 2,

$$B_c \propto \frac{S^{3/4}}{N_c} \tag{2}$$

.

Every gene execution consumes energy. By specifying the amount of energy for every gene, and by establishing E_0 , a thermodynamic size limit can be specified for the phenotypes, as shown in Equation 3. The specification of energy needs to be determined by the user based on his experience with the model. Our experience suggest that the model is not sensitive to these definitions,

$$E_c = E_0 \frac{S^{3/4}}{N_c} \tag{3}$$

.

The advantage of using this approach is that there is no predefined upper bound or other limit on the size of the phenotype. Even when the phenotype reaches the thermodynamic limit, this approach will permit new mass to be created at the expense of removing existing mass, potentially changing the topology of the phenotype.

However, the thermodynamic balance will not prevent phenomena such as unlimited cell division or extermination of the entire phenotype. These last phenomena are addressed by evolution and disease mechanisms. Every phenotype may suffer from a disease during its developmental stage.

3.3 Diseases

A disease, can only occur as a consequence of a defective genome. Examples of diseases in phenotypes include: unlimited production of cells. or production of cells that are significantly distorted. Once a disease has been detected, an artificial immune system attempts to eliminate it using several methods (*e.g.*, refining the mesh). If none of these methods work, the phenotype itself is eliminated, but not before it is evaluated and penalized for being incapable of reaching maturity.

4. RESULTS

4.1 Evolutionary Scheme

The evolutionary scheme is derived from a genetic algorithm. The algorithm is initialized with a set of randomly generated genomes. Starting from a single artificial cell, one individual is grown from each genome by executing the rules it contains. Once each individual reaches maturity, its fitness is evaluated by means of the finite element analysis. The fitness values are used to select parents to produce offspring, where a higher fitness value results in a higher probability of being selected. Once two parents have been selected, they produce offspring through a crossover process. In this process, the genome from each parent is cut at a randomly selected word boundary. A gene string from each parent is joined together producing a child; the remaining gene string from each parent are joined, producing a second child. Similar to evolution in nature, the genome is subject to random mutation. The mutation process can erase an entire word and replace it with another, or replace a single gene within a word. These three steps: selection, crossover and mutation are repeated, and each repetition is defined as

one generation.

4.2 Structural Growth

The approach outlined above has been applied to two experiments representative of an important problem in engineering and nature. The first problem was to synthesize the configuration of a structure to support a highly varied load generated by a wind. In addition, the structure needs to reach a certain height. For this problem, two morphogens are present in the environment. One represents a source that provides an incentive for phenotypes to grow toward it. This source is the desired height of the structure. The second represents the ground. In addition to the two morphogens, the phenotypes are exposed to external forces. The first one is gravity, which is generated equally on all of the cells. The second force is similar to the forces generated by wind, which are proportional to the surface area of the phenotypes. In our model the wind is not constant but rather changes randomly during the growth process. The second experiment was same as the first with slight changes. We reduced the magnitude of the force generated by the wind and added an additional force generated at the location of the source morphogen.

The evaluation of the phenotypes in both experiments was done only in their maturity stage. The fitness evaluation function was composed of six parameters: distance of the phenotype from the light source; age of the phenotype; weight; cell morphology; cell volume; and, the maximum mechanical stress on the cells. All of these parameters were aggregated to a single scalar. The idea behind this experiment was to study the correlation between the development process of phenotypes and their performance in a high volatility environment. Figure 4 and Figure 3 show the developmental process of two phenotypes corresponding to experiments 1 and 2 respectively. Both phenotypes evolved for 1000 generations. The figures show how each phenotype developed from a single cell until it reached maturity. The change in the environment between the two experiments made the evolved configuration of the two phenotypes different. The phenotype in Figure 3 is more condensed, as opposed to the phenotype in Figure 4 which grew branches that tended to spread out. Nevertheless, the growth process for both phenotypes is similar. We can learn from both figures that new mass was created rapidly in early stages of development and decaying slowly as the phenotypes reached maturity. Figure 2 shows the developmental processes of both experiments after 1000 generations. Even though the phenotypes in both experiments were distinguished in terms of size and topology, the slopes of both graphs are similar. In other words, every phenotype matured differently in terms of size and topology with respect to the environment but, the rate of creation of new mass was preserved. In Figure 5 the genome or the DNA of the phenotype in experiment 2 is presented. The red and the yellow colors correspond to "veto" genes serving as control mechanism inside the genome. Although the genome itself is very complex, a large part of it is composed of control growth genes. These "genes" represents the immune and the control systems. it can be seen that these systems has been evolved simultaneously with the phenotypes. These systems enable a corresponding phenotype to reach a maturity stage in a stable process until it finally decays and no additional mass is created. This fact also supports other research in biology which claims that most of the active DNA in an organism is composed with control elements which control growth and other processes.

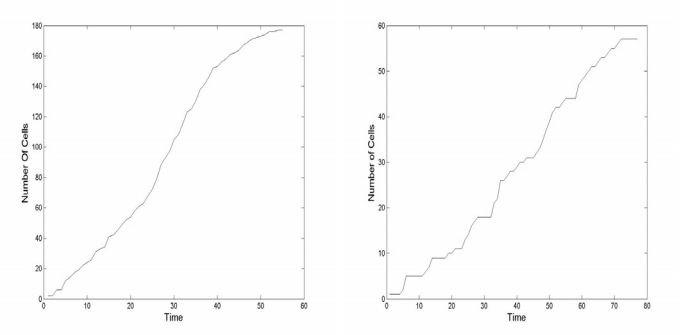
Table 1: Geometrical operation genes

ID	**Name**	N^1	**Possible Parameters**
A	Shear	1	$(d, e, f, i)\times$ fractional coefficient
B	Anisotropic growth	3	$(a, b, c, g, h)\times$ fractional coefficient
C	Isotropic growth	1	$(a, b, c, g, h)\times$ fractional coefficient

[1] N =Number of Parameters

4.3 Discussion and Conclusion

This paper has presented a novel approach for computational embryogeny of three dimensional structures. Our method mimics three control processes from biology (diseases, thermodynamic balancing and control genes). The utilization of these processes lead to evolution of phenotypes that not only performed well under the environment but also



Experiment 1 Experiment 2

Figure 2: Growth plot - number of cells Vs. time. The figure shows a plot of the number of cells verses time, even though the phenotypes in Figure 4 and Figure 3 are different, their growth behavior is similar.

Table 2: Cell type operation genes

ID	Name	N^1	Possible Parameters
D	Cell division	1	(d, e, f, i)
K	Cell death	0	
F	Cell differentiation	0	

[1] N =Number of Parameters

Table 3: Veto(conditional) genes

ID	Name	N^1	Possible Parameters
V	Suppress below	1	$(a, b, c, g, h)\times$ fractional coefficient
W	Suppress above	1	$(a, b, c, g, h)\times$ fractional coefficient

[1] N =Number of Parameters

Table 4: Cell information

ID	Description
a	Maximum principal stress normalized with the yield stress
b	Middle principal stress normalized with the yield stress
c	Minimum principal stress normalized with the yield stress
d	Principal vector correspond to the maximum principal stress
e	Principal vector correspond to the middle principal stress
f	Principal vector correspond to the minimum principal stress
g	Cell volume
h	Morphogen gradient direction
i	Morphogen gradient intensity
t	Time

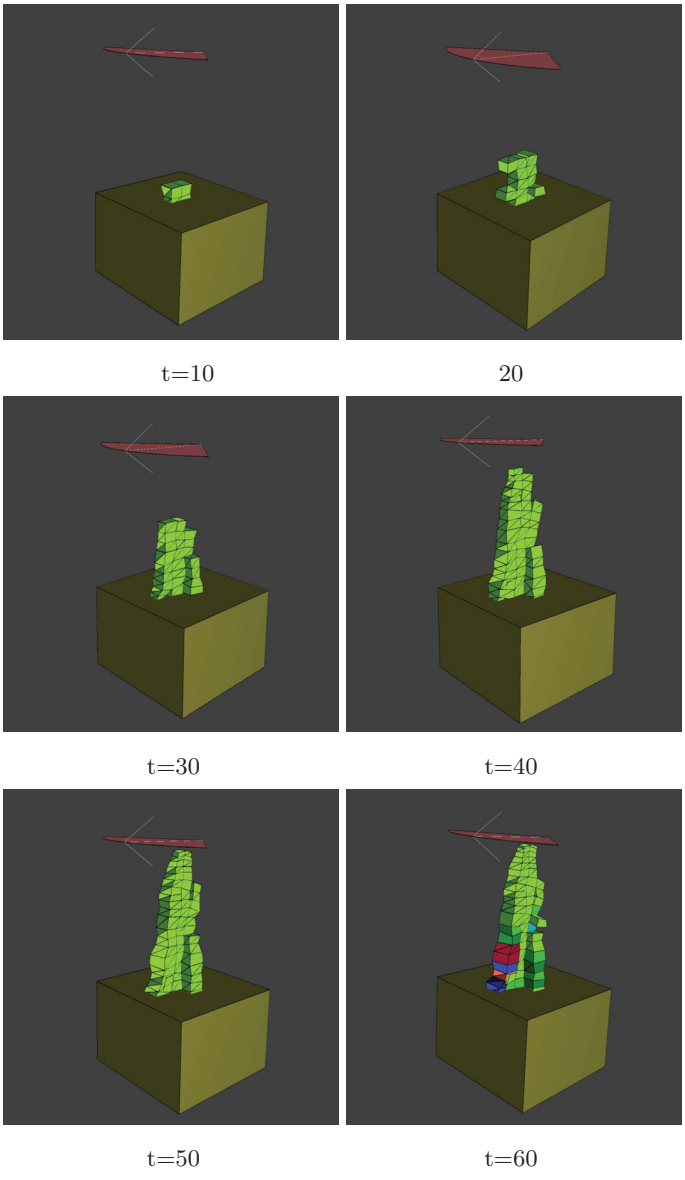


Figure 3: A growth process - second experiment. The figure demonstrate a growth process of the best phenotype in the population in terms of performances. The colors in the images indicates the mechanical stress on the phenotype. Green indicates low stress while red indicate high stress. The creation of new mass was highly rated during the initial stages of development(t=10 - t=40) and was decaying close to the maturity time. The phenotype was capable of supporting all three types of loads since no cell is over stressed.

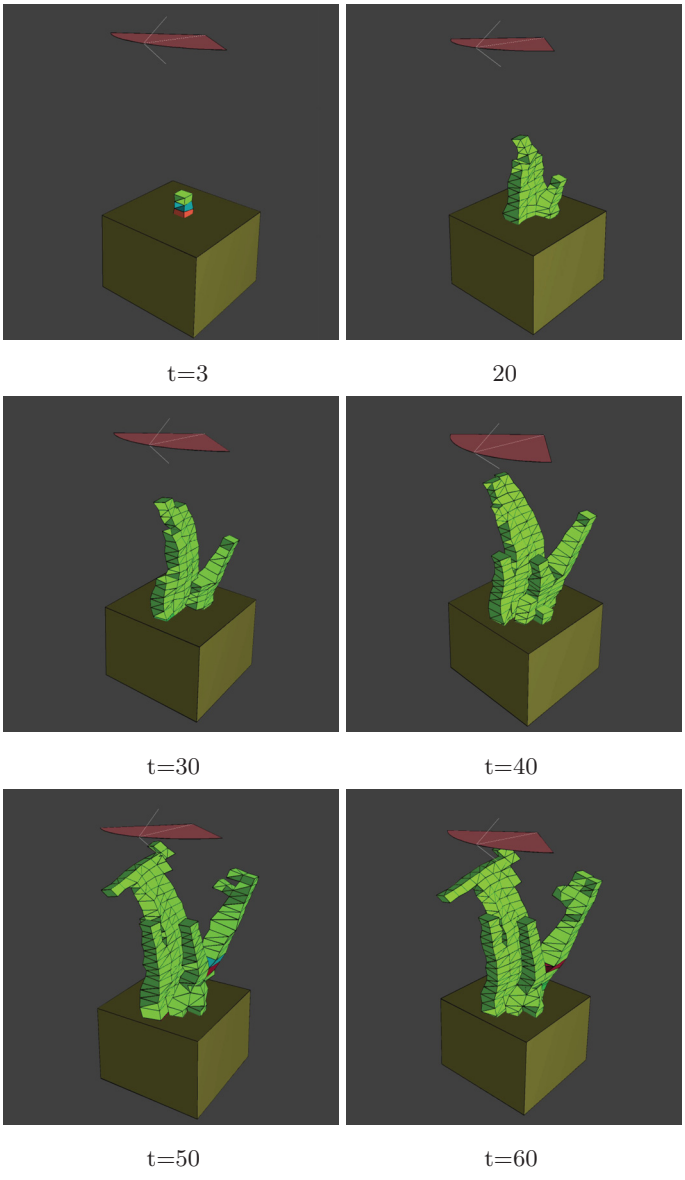


Figure 4: A growth process - first experiment. The figure demonstrate a growth process of the best phenotype in the population in terms of performances. The colors in the images indicates the mechanical stress on the phenotype. Green indicates low stress while red indicate high stress. The creation of new mass was highly rated during the initial stages of development(t=3 - t=40) and was decaying close to the maturity time. The phenotype was capable of supporting all three types of loads since no cell is over stressed.

Figure 5: The genome of the phenotypes in experiment 2. The red and the yellow colors correspond to "veto" genes which control the development process of the phenotype.

Figure 6: A sample figure.

lead to growth and developed via a controlled process. Our results indicate a high correlation between the performance of the phenotype regarding the environment and its ability to grow in a stable manner. We have also found that a large part of the genome was composed of control genes. This result is supported with research from biology.

5. ACKNOWLEDGMENTS

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